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Chronic Toxicity of Lead and Cadmium II. Changes in the Central Nervous System of the F1 Generation of Rats after Chronic Intoxication with Lead and Cadmium

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by

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16. ABSTRACT

This paper examines the effects of chronic exposure to the trace elements, lead and cadmium, on the central nervous system of F_1 generation Wistar rats. Both the parental and F_1 generation received treatments consisting of two levels of lead (5 or 50 ppm), two levels of cadmium (0.1 or 5 ppm), and two combined dosages (5 ppm lead and 0.1 ppm cadmium, or 50 ppm lead and 5 ppm cadmium). Treatments were administered in buffered drinking water.

Behavioral changes, as measured by locomotor activity, were found to be both dose and age dependent. Changes in brain biogenic amino levels were also both dose and age dependent. In general, lead treatment caused decreases in blood aminolevulinic acid dehydrotase while cadmium caused increases in brain acetylcholinesterase and monamine oxidase.

This study suggests that both behavior and biogenic amine level changes in discrete brain areas can occur as early as 30 days of age and these changes may be sensitive signs of chronic exposure to lead and/or cadmium.

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FOREWARD

The many benefits of our modern, developing, industrial society are accompanied by certain hazards. Careful assessment of the relative risk of existing and new man-made environmental hazards is necessary for the establishment of sound regulatory policy. These regulations serve to enhance the quality of our environment in order to promote the public health and welfare and the productive capacity of our nation's population.

The Health Effects Research Laboratory, Research Triangle Park, conducts a coordinated environmental health research program in toxicology, epidemiology, and clinical studies using human volunteer subjects. These studies address problems in air pollution, non-ionizing radiation, environmental carcinogenesis and the toxicology of pesticides as well as other chemical pollutants. The Laboratory participates in the development and revision of air quality criteria documents on pollutants for which national ambient air quality standards exist or are proposed, provides the data for registration of new pesticides or proposed suspension of those already in use, conducts research on hazardous and toxic materials, and is primarily responsible for providing the health basis for non-ionizing radiation standards. Direct support to the regulatory function of the Agency is provided in the form of expert testimony and preparation of affidavits as well as expert advice to the Administrator to assure the adequacy of health care and surveillance of persons having suffered imminent and substantial endangerment of their health.

This paper examines the effects of chronic exposure to the trace elements, lead and cadmium, on the central nervous system of the F_1 generation Wistar rats. Because both lead and cadmium are found in many environments, determining the behavioral effects of these elements is important to humans as well.

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ABSTRACT

This paper examines the effects of chronic exposure to the trace elements, lead and cadmium, on the central nervous system of F_1 generation Wistar rats. Both the parental and F_1 generation received treatments consisting of two levels of lead (5 or 50 ppm), two levels of cadmium (0.1 or 5 ppm), and two combined dosages (5 ppm lead and 0.1 ppm cadmium, or 50 ppm lead and 5 ppm cadmium). Treatments were administered in buffered drinking water.

Behavioral changes, as measured by locomotor activity, were found to be both dose and age dependent. Changes in brain biogenic amino levels were also both dose and age dependent. In general, lead treatment caused decreases in blood aminolevulinic acid dehydrotase while cadmium caused increases in brain acetylcholinesterase and monamine oxidase.

This study suggests that both behavior and biogenic amine level changes in discrete brain areas can occur as early as 30 days of age and these changes may be sensitive signs of chronic exposure to lead and/or cadmium.

SECTION 1

INTRODUCTION

Lead (Pb) and cadmium (Cd) are hazardous trace elements found in the present environment of man. Taking into account possible individual and synergistic effects of chronic exposure to Pb and/or Cd, we have previously studied the effect on the central nervous system in rats chronically exposed to drinking water containing Pb and/or Cd in trace amounts. We have shown that a brief Pb and/or Cd exposure affects the subtle functions of the nervous system (7). In this paper we present the changes in behavior and biogenic amine concentrations in discrete brain areas of rats from the F_1 generation.

SECTION 2

MATERIALS AND METHODS

Forty day old male and female Wistar rats, (Central Animal Farm of the Silesian Academy of Medicine) received one of the following treatments in their drinking water: Group I (control), 0.005 M acetate buffered drinking water; Group II, 5 ppm Pb; Group III, 50 ppm Pb; Group IV, 0.1 ppm Cd; Group V, 5 ppm Pb and 0.1 ppm Cd; Group VI, 50 ppm Pb and 5 ppm Cd. Pb and Cd acetate salts were dissolved in drinking water buffered to pH 7 with an 0.005 M acetate buffer. Animals were exposed for 40 days and pregnant females continued on these regimens throughout gestation and lactation. Rats born from these animals (F_1 generation) were similarly exposed for 40 days beginning 20 days after birth. Each control and experimental group of animals of the F_1 generation consisted of 10 rats. All evaluations described were made at 30, 60 and 90 days of age.

BEHAVIOR

Individual rats were placed in a photocell actometer (9) for 24 hours. They had access to standard laboratory feed and water for 1/2 hour following 6, 12 and 24 hours of testing. Impulses elicited by locomotions were noted from counters every 12 hours (8 p.m. and 8 a.m.).

BIOGENIC AMINES ASSAYS

Rats were killed by cervical dislocation at the end of each experimental period. The brains were quickly removed and placed on Petri dishes filled with ice. Brains were dissected into hypothalamus, pons and medulla oblongata (brain stem), hippocampus with nucleus accumbens (limbic system), and striatum, according to Glowinski and Iversen (6). Spectrophotofluorometric analysis of noradrenaline (NA), 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) concentrations were done according to Miller et al. (11), and dopamine (DA) concentrations according to Cox et al. (3). Fluoroscence was measured using Aminco-Bowman Spectrophotofluorometer.

BIOCHEMICAL STUDIES

Blood samples were collected from animals under light ether anesthesia by heart puncture into heparinized syringes. Following blood collection, the carotid and subclavian arteries were perfused with 60 ml of saline cooled to 4°C. The brain was removed and immediately frozen in dry ice, weighed and homogenized in 5 parts of 0.067 M sodium phosphate

buffer, pH 7 (4) in a teflon homogenizer and then placed in a beaker filled with ice. Amniolevulinic acid dehydratase E.C.4.2.1.24 (ALAD) activity was measured according to Nikkonen et al. (12). Lactate dehydrogenase E.C.1.1.1.27 (LDH) activity was measured spectrophotometrically using UV-test (UV-test [Fermognost, DGR]). Alkaline phosphatase E.C.3.1.3.1

(AlPh) activity was estimated according to Bessey et al. (2). Brain acetylcholinesterase E.C.3.1.1.7 (AChE) activity was measured according to Ellman et al. (5). Brain monoamine oxidase E.C.1.4.3.4 (MAO) activity was measured according to McEven and Cohen (10) using benzylamine (Riedel de Hoen, FRG) as a substrate. Free erythrocyte porphyrine (FEP) was estimated by the method of Piomelli (14), using protoporphyrin IX as the Zn complex and protosol solvent (Porphyrin Products, Logan, Utah). Results were statistically analyzed using the Student t-test.

SECTION 3

RESULTS

BEHAVIOR

Locomotor activity from all treatment groups during Pb/Cd exposure is reported as a percentage of control values (Table 1). Increased diurnal and nocturnal locomotor activity was evident in 30-day old rats treated with 5 ppm Pb, while at 60 and 90 days a decrease in these activities were observed. Fifty ppm Pb treatment increased diurnal locomotor activity in 30-, 60-, and 90-day old rats. In 90-day old rats there was an evident decrease in nocturnal activity. Cd (0.1 ppm) also increased locomotor activity of 30-day old rats, while the diurnal activity in 60- and 90-day old animals was decreased. Changes in locomotor activity after Cd exposure (5 ppm) were seen as an increase of nocturnal activity in 30-day old rats. After simultaneous treatment with lower doses of Pb and Cd, an increase in activity of 30-day old animals was observed and a decrease in diurnal and noctural activity of 90-day old rats was observed. Higher doses of Pb and Cd in 60-day old rats produced a depression in locomotor activity.

BIOGENIC AMINES IN DISCRETE AREAS OF BRAIN

Regional brain NA and DA concentrations are presented in Tables 2 and 3. Overall, the intoxication by Pb caused a decrease in NA content in the examined brain areas while Cd caused an increase. Pb and Cd applied concomitantly in lower doses caused an increase in NA in 30- and 90-day old animals. Higher doses usually caused a decrease of NA in 30- and 60-day old rats and an increase in 90-day old animals.

After 5 ppm Pb, DA level in the striatum increased in 30- and 60-day old animals. Exposure to 50 ppm Pb decreased striatal DA in 30- and 60-day old rats and increased DA in 90-day old rats. Cd (0.1 ppm) increased striatal DA concentrations in 30-day old rats and decreased it in 60- and 90-day old animals. Cd (5 ppm) increased DA in 60-day old rats. Combined Pb and Cd exposure to lower concentrations significantly increased DA in 30-day old rats, while exposure to 50 ppm Pb and 5 ppm Cd increased striatal DA in 30- and 60-day, but not in 90-day old rats.

In general, treatment with 5 ppm Pb decreased 5-HT and increased 5-HIAA in discrete areas of the brain (Tables 4 and 5). Thirty-day old rats exposed to 50 ppm Pb showed an increase in 5-HT and 5-HIAA in the brain stem while a decrease in 5-HT was observed in the limbic system. In 60- and 90-day old rats, exposed to 50 ppm Pb, 5-HT and 5-HIAA levels were increased in discrete areas of the brain.

Increased striatial 5-HIAA was noted in animals receiving 0.1 ppm Cd. In 60-day old rats, a decrease in 5-HT in the hypothalamus, limbic system, and brain stem were seen. Decreased 5-HIAA in the hypothalamus and striatum was also observed in these 60-day old animals. In 90-day old rats, an increase of striatal 5-HT and a decrease of 5-HIAA in the hypothalamus, limbic system, and striatum were seen.

An increase in brain stem 5-HT and 5-HIAA was observed in 30-day old rats treated with 5 ppm Cd. In 60-day old rats, the level of 5-HT decreased in the brain stem and limbic system while the 5-HIAA level increased in the brain stem and limbic system. Increased 5-HIAA levels were found in the limbic system and striatum of 90-day old animals.

Effects of the combined Pb-Cd exposures were primarily synergistic or protective and were not related to age or dose.

BIOCHEMICAL CHANGES

ALA-dehydratase activity in the blood was significantly decreased and free erythrocyte porphyrins were significantly increased in Pb-treated rats (Table 6). AChE and MAO activity in whole brain were variously affected in rats intoxicated by Cd and/or Pb (Table 6). LDH activity and AlPh activity were not significantly changed in any examined group of animals.

SECTION 4

DISCUSSION

Our behavioral studies have shown that both Pb and Cd alter locomotor activity. In control animals, age had no effect on either diurnal or nocturnal activity. In animals treated with Pb or Cd singly there was no pattern to the alterations in locomotor activity with dose or age at testing. When treated with the Pb-Cd combination, 30-day activity was generally elevated; whereas, 60- and 90-day activity was depressed. These CNS mediated activity changes seen in laboratory animals are similar to the clinical syndrome of Pb intoxication in children. Studies have reported that in the absence of any apparent central nervous system toxicity, many children with either asymptomatic or mild lead poisoning show central excitatory symptoms: restlessness; short attention span; easy distractibility; impulsiveness; and apparent purposeless activity (17); whereas severe intoxication causes encaphalopathy (1,8).

Sauerhoff and Michaelson (16) observed that newborn rats suckling dams eating a diet containing 4% lead carbonate displayed hyperactivity, aggressiveness and excessive stereotyped behavior starting at 4 weeks of age. Dopamine level in the whole brain of these rats was decreased 20%, but noradrenaline content remained unchanged. On the other hand, Cutler (4) has found that the frequency and duration of social and sexual investigation was significantly lower in mice exposed to 0.1% lead acetate in drinking water from infancy. Moreover, in lead-treated males, agonistic behavior was also reduced. Reiter et al. (15) have shown that rats exposed to low levels of Pb from conception until adulthood had a delay in nervous system development. As adults, these animals exhibited hypoactivity and decreased responsiveness to amphetamine. Rats of the parental generation demonstrated an equivalent increase in locomotor activity after exposure to lower concentrations of Pb (5 ppm) and/or Cd (0.1 ppm). There was an apparent inhibition of this activity after higher doses of Pb (50 ppm) and/or Cd (5 ppm) were administered (7). Taking into account that normal rats displayed higher locomotor activity during the night than during the day, our results indicated that both metals disturbed the circadian rhythm of locomotor activity, especially in 60- and 90-day old rats.

Many studies have been conducted to establish the influence of Pb on NA and DA levels in the central nervous system, but they were carried out primarily on whole brain preparations. Changes in the serotoninergic

system of the brain after Pb or Cd intoxication have not been investigated systematically. Therefore, we have studied the level of NA, DA, and also 5-HT and the level of its metabolite (5-HIAA) in discrete areas of the rat brain. Cd affected NA level in the early stage of the animal's development. Since this effect disappeared in older animals, two possibilities should be taken into consideration: the increased absorption of Cd before weaning; or adaptation of the older organism to toxic influence. The first explanation is weak because milk does not appear to be an important source of neonatal Cd exposure (13). But the possibility of great susceptibility of developing brains to trace amounts of Cd cannot be excluded. Striatum DA was significantly affected by Pb, Cd, and age of the animals.

In conclusion, it may be said that behavioral and biogenic amine changes in discrete brain areas are probably early and sensitive signs of Pb and Cd intoxication. The lack of correlation between the dose and the time of exposure to toxic agents and the profile of biochemical changes in the brain indicate the unspecificity of the toxicity of Pb and Cd. The same studies are in progress with rats of the F_2 generation.

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TABLE 1

Locomotor Activity Changes (Percent of Control)[a]
Following Exposure to Lead and/or Cadmium

Measurement Time	Age (Days)	Control (Counts/12 hr ± S.D.)	5 ppm Pb	50 ppm Pb	0.1 ppm Cd	5 ppm Cd	5 ppm Pb + 0.1 ppm Cd	50 ppm Pb + 5 ppm Cd
Day	30	929 ± 118	181[b]	142[b]	163[b]	84	132[c]	87
	60	1096 ± 105	87	161[b]	68[c]	107	82	61[b]
	90	950 ± 89	80	120	73[c]	124[c]	63[c]	99
Night	30	1690 ± 182	280[b]	90	186[b]	183[b]	161[b]	132[c]
	60	1708 ± 175	44[b]	138[b]	116	85	88	48[b]
	90	1670 ± 152	65[c]	62[c]	95	112	54[b]	91

a - n = 10 for all groups
b - $p < 0.01$
c - $p < 0.05$

TABLE 2

Noreadrenalin (NA) Changes (Percent of Control)[a]
Following Chronic Exposure to Lead and/or Cadmium

Brain Area	Age (Days)	Control NA Concentration (µg/g ± S.E.)	5 ppm Pb	50 ppm Pb	0.1 ppm Cd	5 ppm Cd	5 ppm Pb + 0.1 ppm Cd	50 ppm Pb + 5 ppm Cd
Hypothalamus	30	2.28 ± 0.08	96	54[b]	105	77[c]	120[c]	90
	60	2.40 ± 0.07	141[c]	56[b]	129[b]	115[c]	92	89
	90	2.30 ± 0.06	95	114	103	103	98	98
Pons plus Medulla	30	0.69 ± 0.02	101	96	89	90	89	74[b]
	60	0.69 ± 0.02	132[b]	99	109	112	95	95
	90	0.67 ± 0.01	120[b]	46[b]	109	88	120[c]	130[b]
Limbic System	30	0.61 ± 0.03	60[b]	50[b]	80[c]	79[c]	71[b]	103
	60	0.59 ± 0.01	135[b]	54[b]	126[c]	113	94	64[c]
	90	0.55 ± 0.01	136[b]	110	103	96	122[c]	125[c]
Striatum	30	0.32 ± 0.04	135[b]	105	85[c]	84[c]	162[b]	84[c]
	60	0.32 ± 0.04	137[b]	113	71[b]	93	98	100
	90	0.31 ± 0.01	135[b]	80[c]	107	104	131[b]	140[c]

a - n = 8 for all groups
b - $p < 0.01$
c - $p < 0.05$

TABLE 3

Dopamine (DA) Changes (Percent of Control)[a]
Following Chronic Exposure to Lead and/or Cadmium

Brain Area	Age (Days)	Control NA Concentration (µg/g ± S.E.)	5 ppm Pb	50 ppm Pb	0.1 ppm Cd	5 ppm Cd	5 ppm Pb + 0.1 ppm Cd	50 ppm Pb + 5 ppm Cd
Striatum	30	5.58 ± 0.33	298[b]	70[b]	402[b]	93[b]	265[b]	133[b]
	60	5.66 ± 0.20	120[c]	62[b]	70[b]	122[b]	90	121[c]
	90	5.14 ± 0.20	118	223	72[b]	85[c]	87	89

a - n = 8 for all groups
b - $p < 0.01$
c - $p < 0.05$

TABLE 4

5-Hydroxytryptamine (5-HT) Changes (Percent of Control)[a]
Following Chronic Exposure to Lead and/or Cadmium

Brain Area	Age (Days)	Control 5-HT Concentration (µg/g ± S.E.)	5 ppm Pb	50 ppm Pb	0.1 ppm Cd	5 ppm Cd	5 ppm Pb + 0.1 ppm Cd	50 ppm Pb + 5 ppm Cd
Hypothalamus	30	2.1 ± 0.1	93	90	95	104	113	114
	60	2.0 ± 0.1	97	103[b]	82[c]	120	92	104
	90	2.0 ± 0.1	92	138[b]	95	101	89	107
Pons plus Medulla	30	0.98 ± 0.04	125[c]	155[c]	108	155[b]	112[b]	119[c]
	60	0.96 ± 0.1	59[c]	47[c]	85	81[c]	185[b]	76[c]
	90	0.91 ± 0.03	86	40[c]	109	97	120[c]	76[c]
Limbic System	30	0.95 ± 0.04	86[b]	70[c]	104[c]	96[c]	167[b]	100[c]
	60	0.93 ± 0.06	70[b]	75[c]	84[c]	88[c]	128[b]	81[b]
	90	0.95 ± 0.05	142[b]	131[b]	102	114	134[b]	69[b]
Striatum	30	0.92 ± 0.02	98[b]	101[c]	110	97	88[c]	130[b]
	60	0.98 ± 0.08	51[b]	73[c]	87[b]	106	115[c]	119[c]
	90	0.93 ± 0.10	107	37[b]	133[b]	100	140[b]	67[b]

a - n = 8 for each group
b - $p < 0.01$
c - $p < 0.05$

TABLE 5

5-Hydroxyindoleacetic Acid (5-HIAA) Changes (Percent of Control)[a]
Following Chronic Exposure to Lead and/or Cadmium

Brain Area	Age (Days)	Control 5-HIAA Concentration (μg/g ± S.E.)	5 ppm Pb	50 ppm Pb	0.1 ppm Cd	5 ppm Cd	5 ppm Pb + 0.1 ppm Cd	50 ppm Pb + 5 ppm Cd
Hypothalamus	30	2.5 ± 0.2	97	96	92	54[b]	102	76[c]
	60	2.3 ± 0.1	72[b]	97	76[c]	119[c]	88	96
	90	2.3 ± 0.1	70[b]	86	43[b]	89	77[c]	74[b]
Pons plus Medulla	30	0.63 ± 0.03	141[b]	170[b]	115[c]	159[b]	73[b]	138[b]
	60	0.61 ± 0.05	165[b]	214[b]	105	145[b]	143[b]	183[b]
	90	0.65 ± 0.02	106	110	129[b]	93	173[b]	97
Limbic System	30	0.62 ± 0.04	91	97	80[c]	151[b]	50[b]	161[b]
	60	0.63 ± 0.04	136[b]	127[b]	107	130[b]	115[c]	127[b]
	90	0.59 ± 0.03	101	88	57[b]	117[c]	119[c]	93
Striatum	30	0.95 ± 0.03	149[b]	174[b]	237[b]	98	95	105
	60	0.09 ± 0.05	125[b]	98	69[b]	97	103	83[c]
	90	1.0 ± 0.1	104	152[b]	65[b]	126[b]	101	77[c]

a - n = 8 for each group
b - $p < 0.01$
c - $p < 0.05$

TABLE 6

Specific Biochemical Changes (Percent of Control)[a]
Following Exposure to Lead and/or Cadmium

	Age (Days)	Control Mean ± S.E.	5 ppm Pb	50 ppm Pb	0.1 ppm Cd	5 ppm Cd	5 ppm Pb + 0.1 ppm Cd	50 ppm Pb + 5 ppm Cd
ALA-	30	121 ± 25	32[b]	15[b]	---	---	21[b]	90
dehydratase	60	48 ± 18	52[b]	73[b]	---	---	25[b]	46[b]
blood	90	49 ± 17	42[b]	71[b]	---	---	50[b]	63[b]
Acetyl-	30	5.8 ± 1.3	146[b]	70[b]	---	---	81[c]	55[b]
cholinesterase	60	6.7 ± 0.5	100	100	152[b]	148[b]	42[b]	80[c]
brain	90	6.0 ± 1.1	62[b]	100	151	180[b]	100	72[b]
Monoamine	30	64 ± 15	330[b]	25[b]	180[b]	100	61[b]	100[b]
oxidase	60	69 ± 19	50[b]	64[b]	160[b]	158[b]	58[b]	170[b]
brain	90	60 ± 15	50[b]	72[b]	158[b]	316[b]	63[b]	176[b]
Free	30	183 ± 58	327[b]	391[b]	---	---	247[b]	290[b]
Erythrocyte	60	103 ± 23	448[b]	412[b]	---	---	473[b]	110
Porphyrins	90	120 ± 15	339[b]	224[b]	---	---	360[b]	318[b]

a - = 8 for each group
b - $p < 0.01$
c - $p < 0.05$

TABLE 4

5-Hydroxytryptamine (5-HT) Changes (Percent of Control)[a]
Following Chronic Exposure to Lead and/or Cadmium

Brain Area	Age (Days)	Control 5-HT Concentration (µg/g ± S.E.)	5 ppm Pb	50 ppm Pb	0.1 ppm Cd	5 ppm Cd	5 ppm Pb + 0.1 ppm Cd	50 ppm Pb + 5 ppm Cd
Hypothalamus	30	2.1 ± 0.1	93	90	95	104	113	114
	60	2.0 ± 0.1	97	103[b]	82[c]	120	92	104
	90	2.0 ± 0.1	92	138[b]	95	101	89	107
Pons plus Medulla	30	0.98 ± 0.04	125[c]	155[c]	108	155[b]	112	119[c]
	60	0.96 ± 0.1	59[c]	47[c]	85	81[c]	185[b]	76[c]
	90	0.91 ± 0.03	86	40[c]	109	97	120[c]	76[c]
Limbic System	30	0.95 ± 0.04	86	70[c]	104	96	167[b]	100
	60	0.93 ± 0.06	70[b]	75[c]	84[c]	88[c]	128[b]	81[c]
	90	0.95 ± 0.05	142[b]	131[b]	102	114	134[b]	69[b]
Striatum	30	0.92 ± 0.02	98	101	110	97	88[c]	130[b]
	60	0.98 ± 0.08	51[b]	73[c]	87	106	115[c]	119[c]
	90	0.93 ± 0.10	107	37[b]	133[b]	100	140[b]	67[b]

a - n = 8 for each group
b - $p < 0.01$
c - $p < 0.05$

TABLE 5

5-Hydroxyindoleacetic Acid (5-HIAA) Changes (Percent of Control)[a]
Following Chronic Exposure to Lead and/or Cadmium

Brain Area	Age (Days)	Control 5-HIAA Concentration (µg/g ± S.E.)	5 ppm Pb	50 ppm Pb	0.1 ppm Cd	5 ppm Cd	5 ppm Pb + 0.1 ppm Cd	50 ppm Pb + 5 ppm Cd
Hypothalamus	30	2.5 ± 0.2	97[b]	96	92[c]	54[b]	102	76[c]
	60	2.3 ± 0.1	72[b]	97	76[c]	119[c]	88[c]	96[b]
	90	2.3 ± 0.1	70[b]	86	43[b]	89	77[c]	74[b]
Pons plus Medulla	30	0.63 ± 0.03	141[b]	170[b]	115[c]	159[b]	73[b]	138[b]
	60	0.61 ± 0.05	165[b]	214[b]	105[b]	145[b]	143[b]	183[b]
	90	0.65 ± 0.02	106	110	129[b]	93	173[b]	97
Limbic System	30	0.62 ± 0.04	91[b]	97[b]	80[c]	151[b]	50[b]	161[b]
	60	0.63 ± 0.04	136[b]	127[b]	107[b]	130[b]	115[c]	127[b]
	90	0.59 ± 0.03	101	88	57[b]	117[c]	119[c]	93
Striatum	30	0.95 ± 0.03	149[b]	174[b]	237[b]	98	95	105[c]
	60	0.09 ± 0.05	125[b]	98[b]	69[b]	97[b]	103	83[c]
	90	1.0 ± 0.1	104	152[b]	65[b]	126[b]	101	77[c]

a - n = 8 for each group
b - $p < 0.01$
c - $p < 0.05$

TABLE 6

Specific Biochemical Changes (Percent of Control)[a]
Following Exposure to Lead and/or Cadmium

	Age (Days)	Control Mean ± S.E.	5 ppm Pb	50 ppm Pb	0.1 ppm Cd	5 ppm Cd	5 ppm Pb + 0.1 ppm Cd	50 ppm Pb + 5 ppm Cd
ALA-	30	121 ± 25	32[b]	15[b]	---	---	21[b]	90[b]
dehydratase	60	48 ± 18	52[b]	73[b]	---	---	25[b]	46[b]
blood	90	49 ± 17	42[b]	71[b]	---	---	50[b]	63[b]
Acetyl-	30	5.8 ± 1.3	146[b]	70[b]	---	---	81[c]	55[b]
cholinesterase	60	6.7 ± 0.5	100[b]	100	152[b]	148[b]	42[b]	80[c]
brain	90	6.0 ± 1.1	62[b]	100	151	180[b]	100	72[b]
Monoamine	30	64 ± 15	330[b]	25[b]	180[b]	100[b]	61[b]	100[b]
oxidase	60	69 ± 19	50[b]	64[b]	160[b]	158[b]	58[b]	170[b]
brain	90	60 ± 15	50[b]	72[b]	158[b]	316[b]	63[b]	176[b]
Free	30	183 ± 58	327[b]	391[b]	---	---	247[b]	290[b]
Erythrocyte	60	103 ± 23	448[b]	412[b]	---	---	473[b]	110[b]
Porphyrins	90	120 ± 15	339[b]	224[b]	---	---	360[b]	318[b]

a - = 8 for each group
b - $p < 0.01$
c - $p < 0.05$